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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,054

11/22/2006

James Pearson

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4648

23405

7590

07/08/2010

HESLIN ROTHENBERG FARLEY & MESITI PC  
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EXAMINER

DESAI, RITA J

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

07/08/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/587,054	<b>Applicant(s)</b> PEARSON ET AL.	
	<b>Examiner</b> Rita J. Desai	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 3-11, 14-16, 18-21 and 24-30 is/are pending in the application.
- 4a) Of the above claim(s) 24-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-11, 14-16 and 18-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/4/06</u> .   | 6) <input type="checkbox"/> Other: _____                          |

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## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I and Group III in the reply filed on 4/28/10 is acknowledged. The traversal is on the ground(s) that Group I should include all the variations a for R1 and R2 and R3 as given in claim 3 as the examiner has not given any reason why the groups are distinct, or burdensome. This is not found persuasive because when a preliminary search of formula I was done it gave numerous iterations, However the claims 3-11, 14-16, 18-21 as amended are now under examination..

The requirement is still deemed proper and is therefore made FINAL..

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

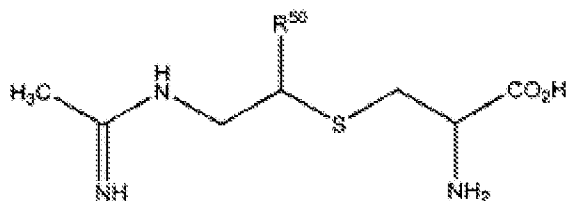
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3-11,14-16,18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvey et al US 20030199529 and all the various documents cited in the specifications on pages

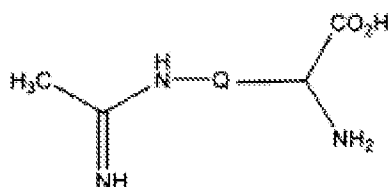
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11-13 of the specifications. And Wang 2002.

inhibitors described in US pat 6,355,689:



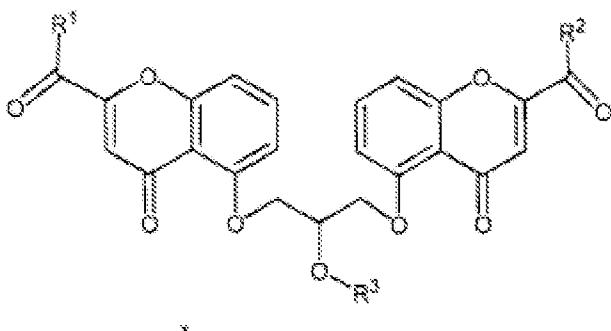
wherein  $R^{50}$  is chosen from  $C_1$  to  $C_6$  alkyl,  $C_3$  to  $C_4$  cycloalkyl,  $C_1$  to  $C_4$  hydroxyalkyl and  $C_1$  to  $C_6$  haloalkyl or US patent 5,863,931:



wherein Q is chosen from  $-\text{CH}_2\text{CH}=\text{CHCH}_2-$ ,  $-(\text{CH}_2)_p\text{V}(\text{CH}_2)_q-$ ,  $-\text{O}-$ ,  $-\text{NR}^{51}-$  and  $-(\text{CH}_2)_r\text{T}(\text{CH}_2)_s-$ ; p is 2 or 3; q is 1 or 2; V is  $\text{S}(\text{O})_x$ ; x is 0, 1 or 2;  $R^{51}$  is H or  $C_{1-6}$  alkyl; r is 1 or 2; s is 1 or 2; and T is cyclobutyl, phenyl or pyridyl. Other iNOS inhibitors useful as parent structures in the instant invention may be found in US patents 6,451,821; 5,132,453; 5,830,917; 5,684,008; 6,207,708; 6,344,473; 6,143,790; 5,866,612; 6,369,272; 6,552,052; 6,495,544; 6,403,830; 5,629,322; 6,110,930; 6,228,866; 6,274,557; 6,432,947; 6,451,821; 5,449,688; 5,723,451; 5,854,251; 5,863,931; 5,889,056; 5,919,787; 5,945,408; 5,972,940; 5,981,511; 6,355,689; 6,423,705; 6,586,474 and 6,465,686; in US published applications 20030013702; 20020037927; 20020049202; 20030119826; 20020022631; 20020198243; 20030064978; 20030195256; 20030207896; 20030109522; 20040087653; in PCT applications WO99/62875; WO99/628785; WO01/78719; WO01/05748;

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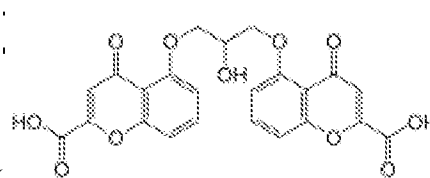
Applicants claims are drawn to compounds of the formula



with R1, R2 and R3 as different groups

which are iNOS inhibitors. The groups have many different structures as can be seen by the claim.

Scope & Content of Prior Art MPEP 2141.01



Garvey discloses similar cromonyl core (

which are

mast cell stabilizers) which are attached to the NO inhibitors. These also treat asthma.

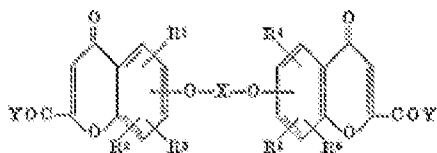
Also see page 2.

[0009] Therefore, one aspect of the invention provides a compound comprising a steroid, a  $\beta$ -agonist, an anticholinergic, a mast cell stabilizer or a PDE inhibitor to which is directly or indirectly linked at least one NO or NO<sub>2</sub> group or a group which stimulates the endogenous production of NO or EDHF in vivo. The groups can be linked through sites such as oxygen (hydroxyl condensation), sulfur (sulfhydryl condensation), carbon and nitrogen.

The various documents cited in the specifications from page 11-13 teach many of the R1-R3 substituents which stimulates production of NO.

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Johnson ( cited in the IDS) teaches similar compounds for treating asthma



Wang teaches that iNOS may contribute to the NO production and regulate  $\text{Na}^+$  and  $\text{HCO}_3^-$  transport activity and thus in turn help in the treatment of Asthma.

(27). These observations support the view that NO upregulates proximal tubule transport under physiological conditions. Although it is not clear what fraction of total NO is produced by individual NO isozymes, the acute inhibition of iNOS by a selective inhibitor and knockout of iNOS reduced  $\text{Na}^+$  and  $\text{HCO}_3^-$  absorption, indicating that iNOS may contribute to the NO produced in the proximal tubule and regulate  $\text{Na}^+$  and  $\text{HCO}_3^-$  transport activity.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

One of skill in the art of drug design would be motivated to attach directly or indirectly various groups that would stimulate the production of NO, according to Garvey et al , and Wang's teaching that iNOS does play a +ve role in the treatment of Asthma, would have been motivated to make compounds which were directly or indirectly attached to a NO inhibitor.

### ***Conclusion***

Claims 3-11,14-16,18-21 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/  
Primary Examiner, Art Unit 1625

July 1, 2010 .